UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,335	01/15/2004	Seth J. Orlow	71369.368 and PFI-016CIPD	6410

23483 7590 02/01/2008

WILMERHALE/BOSTON
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

michael.mathewson@wilmerhale.com
teresa.carvalho@wilmerhale.com
sharon.matthews@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	10/758,335	ORLOW ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 56 and 69 are presented for examination

Applicants' amendment filed 10/12/2007 has been received and entered into the application. Accordingly, claims 56 and 69 have been amended and claims 47-49, 51-55, 60-62, and 64-68 have been cancelled.

Applicants' arguments have been fully considered and are persuasive to overcome the rejections of record. Accordingly, rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

In light of the new rejections being applied against the pending claims, which were not necessitated by Applicants' amendments, this Office Action is **Non-Final**.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 1/24/2008. The Examiner has considered the references cited therein to the extent that each is a proper citation. USP No. 3,389,051 was not considered because it was previously considered (PTOL 1449 mailed 7/6/2006) and cited in the IDS filed 2/20/2004. Reference CF was not considered because International Search Reports are not considered to be "published" non-patent literature by the USPTO. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56 and 69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Newly introduced claim limitations reciting administration of "one or more compounds" lack support in the specification as filed. The originally filed claims only disclosed administration of "a compound". Further, the invention as described in the originally filed specification (*e.g.*, page 7, line 2 and page 11, line 5) only cites treatment with "a compound" (*i.e.*, there is no suggestion or teaching in the specification that Applicants contemplated administering a plurality of the claimed compounds).

Accordingly, there is no written basis for the newly added plural limitation "or more compounds" as recited in amended claims 56 and 69.

Claims 56 and 69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decreasing melanin content in a melanocyte and/or decreasing skin pigmentation comprising administering a claimed compound of formulas II-VIII, does not reasonably provide enablement for decreasing melanin production in a melanocyte

and/or for effecting an alteration in late endosomal/lysosomal trafficking comprising administering a claimed compound of formulas II-VIII. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 56 and 69 recite methods of decreasing melanin production in a melanocyte (claim 56) or decreasing skin pigmentation (claim 69), comprising administration of "an effective amount of a compound that effects an alteration in late endosomal/lysosomal trafficking" wherein the compound has the formula II, III, IV, V, VI, VII, or VIII as recited in claims 56 and 69. The claimed effect of administration of one of the compounds of the invention is decreased melanin production in a melanocyte (claim 56) or reduced skin pigmentation (claim 69).

The amount of direction or guidance presented: Although the specification discusses methods of measuring melanin content in melanocytes (e.g., pages 47-51 in Section 2.2 and Example 6 at pages 78-79), it does not provide cellular assays or working examples to guide the skilled artisan to determine whether the claimed compounds decrease melanin production *per se* or effect an alteration in late endosomal/lysosomal trafficking as instantly claimed. While Applicants have demonstrated that some of the claimed compounds decrease the total melanin content in melanocytes and do not alter tyrosinase activity *in vitro*, there is no indication, other than unsupported speculation, that the claimed compounds decrease the actual production of melanin or have an effect on late endosomal/lysosomal trafficking as recited in the instant claims. Thus, the specification fails to provide sufficient enablement for decreasing melanin production in a melanocyte or effecting an alteration in late endosomal/lysosomal trafficking.

The state and predictability of the art: There is no evidence of record that an *in vitro* measurement of total melanin content in a melanocyte is a predictable measurement of melanin production *per se*, or whether a compound effects an alteration in late endosomal/lysosomal trafficking. For example, melanin could reasonably be produced in normal quantities in the presence of the claimed compounds and simply be degraded by the cells, which would result in decreased total melanin content per Applicants' disclosed testing procedure, but would not be indicative of decreased melanin production or an alteration in late endosomal/lysosomal trafficking. Whether or not any particular claimed compound effects a decrease in melanin production or an alteration in late endosomal/lysosomal trafficking requires a cellular or *in vivo* assay capable of measuring the effects of said compounds on melanin production or late

endosomal/lysosomal trafficking. In the instant case, Applicants have provided no such assays that would enable one skilled in the art to measure the claimed activity of the recited compounds.

The relative skill of those in the art: Absent sufficient guidance from Applicants (discussed *supra*), even with advanced training the skilled artisan would have to engage in extensive research to practice the claimed methods of decreasing melanin production *per se* or effecting an alteration in late endosomal/lysosomal trafficking by administering the claimed compounds of formulas I-VIII.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The instantly claimed methods require several criteria: (1) the compounds being administered must result in decreased melanin production in a melanocyte (claim 56); (2) the claimed compounds must also effect an alteration in late endosomal/lysosomal trafficking (claims 56 and 69); (3) the claimed compounds must result in reduced skin pigmentation (claim 69). While Applicants have demonstrated that administration of the claimed compounds to melan-a melanocytes results in a decrease in total melanin content in said cells, there is no evidence of record that administration of the claimed compounds decreases melanin production *per se* or that they effect an alteration in late endosomal/lysosomal trafficking.

As such, Applicants' disclosure, specifically the working examples, is not commensurate in scope with the claimed methods of decreasing melanin production or effecting an alteration in late endosomal/lysosomal trafficking.

Claim Rejections - 35 USC § 102

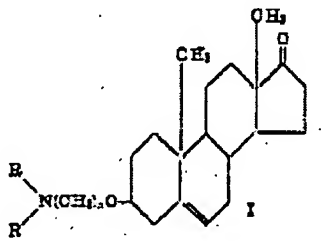
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by **Kagan** (USP No. 3,389,051; Issued June 18, 1968) (prior art of record).

The instant claims recite a method of decreasing melanin production in a melanocyte (claim 56) or a method of reducing skin pigmentation (claim 69) comprising administering one or more compounds of formulas II-VIII. It is further recited in the claims that the compounds effect and alteration in late endosomal/lysosomal trafficking.

Kagan teaches compounds of formula I wherein R is an alkyl group of less than 4 carbons and n is an integer of 2-6 (col. 1, lines 21-69), which reasonably discloses a compound inclusive of a compound as set forth in the instant claims (compound VIII).



The compounds of Kagan are taught to be useful in significantly reducing the cholesterol content of both blood and tissue by partially arresting the biosynthesis of cholesterol in the body (col. 2, lines 36-40). For administration to humans, Kagan teaches administration in unit dosage forms such as tablets, pills, capsules, powders, wafers, cachets, granules, sterile parenteral solutions or

suspensions in aqueous or oil vehicles, oral aqueous or oil dispersions, including syrups and elixirs, and the like (col. 4, lines 69-75).

Kagan does not explicitly teach the specifically claimed compound of formula VIII and is silent with respect to decreasing melanin production in a melanocyte or reducing skin pigmentation.

However, if one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. In re Petering, 301 F.2d 676, 133 USPQ 275 (CCPA 1962). In the instant case, preferred embodiments of Kagan are compounds wherein R is ethyl, thus leading one skilled in the art to immediately envisage such a substituent, which is the same substituent recited in the compound of formula VIII in the instant claims. See Preparation 1 of Kagan (col. 3, lines 22-48). With respect to the stereochemistry of the compound of formula VIII recited in the instant claims, in the compounds of formula I taught in Kagan, there are only 4 possible stereoisomers involving the methyl substituents attached to the ring system (*i.e.*, *RR*, *RS*, *SR*, or *SS*). As such, one skilled in the art could immediately envisage the stereochemistry as recited in the claimed compound of formula VIII.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly

claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Though Kagan does not expressly teach decreasing melanin production in a melanocyte (claim 56) or reducing skin pigmentation (claim 69) as a result of the administration of the disclosed compounds to either the subject or the cell cultures, the administration of the same compound(s) as claimed (*e.g.*, those identical to Applicant's claimed compound of formula VIII where R is ethyl) to the same host (*i.e.*, human or human cell) as claimed is considered to necessarily have the claimed effect of decreasing melanin production in a melanocyte (claim 56) or reducing skin pigmentation (claim 69), on the subject or cell being treated, whether expressly recognized by Kagan or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

Further, the instant claims lack any patient population limitation and thus administering a compound of formula I to a patient in need of cholesterol reduction as taught in Kagan reasonably reads on the instant claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

January 28, 2008

Ardin H. Marschel 1/29/08

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER